

REMARKS**The 35 U.S.C. §103 Rejections**

Claims 1, 7-9 and 11 remain rejected under 35 U.S.C. §103(a) as unpatentable over **Mehta et al.** (*Proceeding of the American Association for Cancer Research*, 38:88, 1997) in view of **Flavell et al.** (*Cancer Research*, 57:4824-4829, 1997). This rejection is respectfully traversed.

Flavell et al. teaches an anti-CD38-saporin immunotoxin but does not teach any methods of enhancing the expression of the target molecule on the surface of a tumor cell. As a result, the anti-CD38-saporin immunotoxin was relatively inefficient and **Flavell et al.** teaches that it must be administered with other immunotoxins to be effective. **Mehta et al.** teaches that retinoids stimulate upregulation of CD38 antigen expression. **Mehta et al.** suggests retinoid stimulation of CD38 antigen expression may have clinical utility in the treatment of certain leukemias but provides no specific means for accomplishing this.

The Examiner argues that even though the anti-CD38-saporin immunotoxin treatment of *Flavell et al.* was relatively ineffective, *Mehta et al.* overcomes its deficiencies by providing a means to upregulation of CD38 antigen expression so that the anti-CD38-saporin immunotoxin would be effective alone. The Applicants respectfully disagree.

Without actually attempting the combination in a manner analogous to that of the instant specification, one of skill in the art would not be able to determine that the retinoid stimulation of CD38 expression would enable the *Flavell et al.* immunotoxin to be used as the sole administered immunotoxin. It is possible that the immunotoxin would have remained ineffective against leukemia cells. Furthermore, the Examiner ignores that fact *Flavell et al.* teaches away from the instant application in emphasizing the simultaneous use of immunotoxins against multiple cellular markers.

Applicants assert that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention absent some teaching, suggestion, or incentive supporting

the combination. In re Bond, 910 F.2d 831, 834 (Fed. Cir. 1990); See also ACS Hospital Systems, Inc. v. Montefiori Hospital, 732 F.2d 1572, 1577 (Fed. Cir. 1984). In suggesting even more complicated cocktails of multiple immunotoxins instead of attempting to enhance the effectiveness of a single immunotoxin, **Flavell et al.** teaches away from the instant invention. As a result, one of skill in the art would not have been inclined to combine the teachings of **Mehta et al.** and **Flavell et al.** Therefore, the Applicants respectfully request that the 35 U.S.C. §103(a) rejection of claims 1-3 and 7-11 over **Mehta et al.** in view of **Flavell et al.** be withdrawn.

Claims 1, 5-9 and 11 remain rejected under 35 U.S.C. §103(a) as unpatentable over **Mehta et al.** (Proceeding of the American Association for Cancer Research, 38:88, 1997) in view of **Flavell et al.** (Cancer Research, 57:4824-4829, 1997), in further view of **Mehta et al.** (Proceeding of the American Association for Cancer Research, 35:92, 1994). This rejection is respectfully traversed.

As argued above, one of skill in the art would not be inclined to combine the teaching of **Mehta et al.** (1997) and **Flavell et al.** to obtain the instant invention because **Flavell et al.** teaches away from methods of enhancing the effectiveness of a single immunotoxin and instead relies on immunotoxin combinations. Furthermore, one of skill in the art would not know whether the combination **Flavell** and **Mehta** would be effective without further, undue experimentation. **Mehta et al.** (1994) merely reports that retinoic acid enhances expression of CD38 in myeloid leukemia cells. **Mehta et al.** (1994) provides no additional teachings to suggest the combination of retinoic acid and a single anti-CD38 immunotoxin would actually be an effective treatment against leukemia or lymphoma. Therefore, the Applicants respectfully request that the 35 U.S.C. §103(a) rejection of claims 1-3 and 7-11 over **Mehta et al.** (1997) in view of **Flavell et al.** in further view of **Mehta et al.** (1994) be withdrawn.

This is intended to be a complete response to the Office Action mailed May 22, 2001. Applicants submit that the pending

claims are in condition for allowance. If any issues remain, please telephone the attorney of record for immediate resolution.

Respectfully submitted,

DATE:

July 9, 2001



Benjamin Aaron Adler, Ph.D., J.D.
Registration No. 35,423
Counsel for Applicant

ADLER & ASSOCIATES
8011 Candle Lane
Houston, Texas 77071
(713) 270-5391
badler1@houston.rr.com